

**REMARKS**

Claims 1-6, 8-18 and 21-27 were pending in this application. Claims 4-6, 8-12, 15-18 and 25-27 have been withdrawn by the Examiner as being drawn to non-elected inventions.

Applicants have amended claims 1 and 22-24 to more particularly point out and distinctly claim the methods of the presently elected invention. Specifically, claims 22-24 have been amended to recite that the amount of agent to be administered is 1.4 to 285 mg per day. Support for the amendment can be found in the specification at, *inter alia*, page 3, lines 17-18. In addition, claim 1 has been amended to recite that the method comprises administering to an animal in need of the bone or cartilage therapy a therapeutically effective amount of an agent comprising creatine pyruvate or analogue thereof. Finally, claim 21 has been amended to correct a minor editorial error. No new matter has been added.

Applicants respectfully request that the amendments and remarks made herein be entered into the record of the instant application. Upon entry of the present amendments, claims 1-6, 8-18 and 21-27 will be pending in the present application.

**I. THE CLAIM REJECTIONS UNDER 35 U.S.C. § 103 SHOULD BE WITHDRAWN**

Claims 1-3, 13, 14, 21-24 remain rejected under 35 U.S.C. § 103(a) (“Section 103(a)”) as allegedly being unpatentable over Kaddurah-Daouk (U.S. Patent No. 5,998,458, “Kaddurah-Daouk”) in view of Meisner (U.S. Patent No. 4,772,591, “Meisner”), Grant *et al.* (U.S. Patent No. 5,888,553, “Grant”), Beale (U.S. Patent No. 5,756,469, “Beale ‘469”), and Beale *et al.* (U.S. Patent No. 5,716,926, “Beale ‘926”). In the Advisory Action mailed January 25, 2006, the Examiner maintains the reasons set forth in the final Office Action mailed September 20, 2005 and additionally alleges that since both creatine and pyruvate are known to be similarly useful against bone disorder, the combination of the two would have been obvious. For the following reasons, Applicants disagree.

As a preliminary matter, Applicants have amended claim 1 to clarify that the subject is in need of treatment of at least one bone or cartilage condition, and amended claims 22-24 to recite that 1.4 to 285 mg of the agent is to be administered per day. Applicants respectfully request that the Examiner reconsider the rejection in view of the amendments made.

To reject claims in an application under 35 U.S.C. § 103, the Patent Office bears the initial burden of establishing a *prima facie* case of obviousness. See *In re Bell*, 26 USPQ2d 1529, 1530 (Fed. Cir. 1993); MPEP 2142. In the case where the claimed ranges “overlap or lie inside ranges disclosed by the prior art” a *prima facie* case of obviousness exists. *In re*

*Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990); *In re Geisler*, 116 F.3d 1465, 1469-71, 43 USPQ2d 1362, 1365-66 (Fed. Cir. 1997). Similarly, a *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties.

Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness with respect to the recited dosage range. See MPEP 2144.05. First, the recited range does not overlap or lie inside any of the ranges disclosed by the prior art. None of the references teach the administration of 1.4 to 285 mg per day of creatine pyruvate, as recited in amended claims 1 and 22-24. Meisner and Grant do not disclose any range. While the other three remaining references disclose some range, the ranges disclosed lie outside of the recited range. For examples, Kaddurah-Daouk discloses that the amount of creatine to be administered is 2 to 8 g (or 2,000 to 8,000 mg) per day (see Kaddurah-Daouk, col. 11, lines 29-31), Beale '469 discloses that the amount of pyruvate compositions to be administered is at least 5 g (or 5,000 mg) per day (see Beale '469, col. 6, lines 8-10), and Beal '926 discloses that the amount of pyruvate compositions to be administered is 1 to 300 g (or 1,000 to 300,000 mg) per day (see Beale '926, col. 5, lines 26-28), all of which are significantly higher than the recited range of 1.4 to 285 mg per day. As such, not only do the references fail to teach the recited range, they also teach away from the significantly smaller amounts recited in amended claims 1 and 22-24.

The recited range is also not close enough to the ranges disclosed by the prior art such that one skilled in the art would have expected them to have the same properties. For example, the high end of the ranges disclosed by the prior art (*i.e.*, 8 g (or 8,000 mg) per day by Kaddurah-Daouk) is close to thirty times greater than the high end of the recited range (*i.e.*, 285 mg per day), whereas the low end of the range disclosed by the prior art (*i.e.*, 1 g (or 1,000 mg) per day by Beale '926) is at least three times greater than the high end of the recited range. Thus, Applicants respectfully submit that the Examiner has failed to make out a *prima facie* case of obviousness with respect to the recited range. As such, amended claims 1 and 22-24, and their dependent claims thereof, are patentable over Kaddurah-Daouk, Meisner, Grant, Beale '469, and Beale '926.

Applicants submit that the pending claims are additionally patentable over Kaddurah-Daouk, Meisner, Grant, Beale '469, and Beale '926 because the target population is different from those in the cited references. A preamble is treated as a limitation if it gives "life and

meaning” to the claim. *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333, 68 USPQ2d 1154, 1157 (Fed. Cir. 2003) (citing *Kropa v. Robie*, 187 F.2d 150, 152 (CCPA 1951)). In *Jansen*, the court held that a claim’s recitation of a patient or a human “in need” gives life and meaning to the preamble’s statement of purpose. 342 F.3d at 1333. More specifically, in *Jansen*, the court held that patent claiming method “for treating or preventing” a particular condition to be performed on a “human in need thereof” requires that the human know that he or she was in need of treatment or prevention of said particular condition. 342 F.3d at 1333.

Claim 1, as amended, requires the animal which is being treated to know that it was in need of the treatment of a bone or cartilage condition. Kaddurah-Daouk does not teach or suggest the administration of creatine pyruvate to a subject who desires treatment of a bone or cartilage condition. Instead, Kaddurah-Daouk discloses the use of creatine compounds for treating or preventing a metabolic disorder related to body weight control such as obesity, and its associated diseases (see Kaddurah-Daouk, Abstract). While Kaddurah-Daouk lists osteoporosis and osteoarthritis as two examples of disorders which relate to obesity (see col. 2, lines 48-49), Kaddurah-Daouk does not teach or suggest the administration of creatine to a subject who desires the specific treatment of osteoporosis or osteoarthritis, but primarily for the purpose of regulating body weight. In *Jansen*, the court reasoned that the “need” must be recognized and appreciated by the subject even though it may be possible that the same need is satisfied without the subject knowing so. 342 F.3d at 1334. Since the subjects of Kaddurah-Daouk desired a type of treatment different than that desired by the subjects of amended claim 1, Kaddurah-Daouk does not render obvious amended claim 1. Moreover, Kaddurah-Daouk discloses a significantly different dosage level than specific by the claim and thus would not teach or suggest use for treatment of a bone or cartilage condition, and certainly not at the specified lower dosage levels.

None of the remaining references cure the deficiencies of Kaddurah-Daouk. While Meisner provides examples of treating subjects with periodontal diseases and osteoarthritis (see, e.g., Examples 6-11), none of the examples involved the use of creatine, much less creatine pyruvate, as recited in amended claim 1. Grant, Beale ‘469 and Beale ‘469 all relate to methods of increasing mass of muscle, which is a different type of body tissue than bone or cartilage. Thus, the subjects in Grant, Beale ‘469 and Beale ‘469 desired a therapy which is different than the therapy intended for the subjects of amended claim 1 and on an all together different body tissue. Thus, amended claim 1 is patentable over the cited references.

For similar reasons, Applicants submit that Kaddurah-Daouk, Meisner, Grant, Beale '469, and Beale '926, either alone or together, also do not teach or suggest the use of creatine pyruvate to promote growth and mineralization of bone or cartilage cells and tissues in a subject in need of such treatment, as recited in amended claim 22. As discussed above, Kaddurah-Daouk relates to regulating body weight of subjects, not the treatment of osteoporosis or osteoarthritis. Based on applicable case law (see, e.g., *Jansen*, 342 F.3d 1329) that stands for the proposition that a preamble that sets forth the objective of a claimed method is to be treated as a limitation if it gives "life and meaning" to the claim, Applicants submit that Kaddurah-Daouk does not teach or suggest the administration of creatine pyruvate to subjects who desire the growth and mineralization of bone or cartilage cells and tissues, as recited in amended claim 22. The remaining references do not cure the deficiency of Kaddurah-Daouk since none of them are directed to promoting growth and mineralization of bone or cartilage cells and tissues. Specifically, Meisner relates to wound healing, and each of Grant, Beale '469 and Beale '926 relates to muscle mass building. As such, none of the cited references, either alone or together, teach or suggest promoting growth and mineralization of bone or cartilage cells and tissues in a subject in need of such treatment, as recited in amended claim 22. Thus, amended claim 22 is patentable over the cited references.

Applicants submit that the teaching of Kaddurah-Daouk, Meisner, Grant, Beale '469, and Beale '926, either alone or together, also do not teach or suggest the use of creatine pyruvate to improve acceptance and osseous integration of bone implants in a subject in need of such treatment, as recited in amended claim 23. As discussed above, Kaddurah-Daouk relates to body weight regulation, Meisner relates to wound healing, and Grant, Beale '469, and Beale '926 relate to muscle building. In fact, none of the references ever mentioned the term "bone implant." Thus, amended claim 23 is patentable over the cited references.

Applicants submit that the teaching of Kaddurah-Daouk, Meisner, Grant, Beale '469, and Beale '926, either alone or together, also do not the use of creatine pyruvate to accelerate healing in a subject having a defect in bone or cartilage tissue caused by trauma or surgery in a subject in need of such treatment, as recited in amended claim 24. While Meisner describes a method to accelerate healing of wounds caused by trauma or surgery (see col. 7, lines 9-10), the method disclosed by Meisner does not use creatine pyruvate, as required by amended claim 24. Since Kaddurah-Daouk, Grant, Beale '469, and Beale '926 never mentioned accelerating healing of bone or cartilage defects caused by trauma or surgery, they do not

remedy the deficiency of Meisner. Thus, amended claim 24 is patentable over the cited references.

Applicants submit that the Examiner has improperly used hindsight reconstruction to pick and choose among isolated disclosures in Kaddurah-Daouk, Meisner, Grant, Beale '469, and Beale '926 to reconstruct the claimed invention. The use of five disparate references from which to pick and choose isolated disclosures without regard to the reference as a whole is indicative of such hindsight reconstruction. In particular, Applicants respectfully submit that *hindsight reconstruction* has been used in the rejection of the present invention to combine a metabolic disorder treatment with a wound healing therapy and a body building regimen. Such hindsight, however, is improper. Hindsight should be avoided in applying the non-obviousness requirement. *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1 USPQ2d 1593 (Fed. Cir. 1987), *cert. denied*, 481 U.S. 1052 (1987).

Furthermore, none of the cited references, either alone or together, teach or suggest each and every claim limitation. The Examiner admits that Kaddurah-Daouk fails to teach or suggest creatine pyruvate (see Office Action at page 2, point no. 4). Meisner, Grant, and Beale '269 also fail to teach or suggest the use of creatine pyruvate. Although Beale '469 discloses pyruvyl-creatine as a pyruvate precursor (see Beale '469, col. 4, lines 39-40), Beale '469 does not teach or suggest using pyruvyl-creatine to treat a bone or cartilage condition, as recited in claim 1; to promote bone growth and mineralization of bone or cartilage cells and tissues, as recited in claim 22; to improve acceptance and osseous integration of bone implants, as recited in claim 23; or to accelerate healing of a defect in bone or cartilage tissue caused by trauma or surgery, as recited in claim 24. Moreover, none of the references teach the dosage amounts specified in claims 1, 22, 23 and 24.

Finally, Applicants submit that there is no suggestion or motivation in any of Kaddurah-Daouk, Meisner, Grant, Beale '469, and Beale '926 to modify or combine the references since they relate to different technical fields. As discussed above, Kaddurah-Daouk relates to a method of treating a metabolic disorder, Meisner relates to a method of healing wounds, and Grant, Beale '469, and Beale '926 all relate to a method of increasing muscle mass. One skilled in the art of metabolic disorder treatment would have no motivation to modify or combine the teaching of Kaddurah-Daouk with Meisner, Grant, Beale '469, and Beale '926. Likewise, one skilled in the art of wound healing would have no motivation to apply the teaching of Kaddurah-Daouk, Grant, Beale '469, or Beale '926 to Meisner. Nor would one skilled in the art of body building have motivation to modify or

combine the teachings of any of Grant, Beale '469, and Beale '926 with Kaddurah-Daouk and Meisner. Therefore, based on these cited references, one skilled in the art would have no reasonable expectation of arriving at the claimed invention.

For the foregoing reasons, Applicants respectfully submit that a case of *prima facie* obviousness has not been established. As such, the rejection under Section 103(a) is in error and Applicant respectfully request that the claim rejections under Section 103(a) be withdrawn.

**CONCLUSION**

Applicants respectfully request entry of the remarks made herein into the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

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Brian M. Rothery  
Brian M. Rothery (Reg. No. 35,340)

By:

Ann W. Chen  
Ann W. Chen (Reg. No. 49,013)  
**JONES DAY**  
222 East 41st Street  
New York, New York 10017  
(212) 326-3939